

Amendment and Response

Applicants: Michael S. KINCH et al.

Serial No.: 09/640,952

Filed: 17 August 2000

For: EPHA2 AS A DIAGNOSTIC TARGET FOR METASTATIC CANCER (As Amended)

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Remarks

The Office Action mailed June 19, 2003, has been received and reviewed. Claims 1, 3, 5, 21, 33-37, 41, 43, 45, 46 and 91 having been amended and claims 28, 30, 31 and 38-40 having been canceled, without prejudice, the claims which are pending and are under consideration are claims 1, 3-13, 21, 23, 24, 33-37, 41-47, 49-69, 72, 73, 75-81, 90 and 91. Of these, claims 72, 73, 75-81, 90 and 91 were indicated as allowable by the Examiner.

Claim 1 has been amended to recite the features recited in claim 28; claim 28 has been accordingly canceled, without prejudice, and claims 34-37, 41, 43, 45 and 46 have been amended to depend from claim 1.

Claim 3 has been amended to delete the term "epitope" which lacked antecedent basis. Claim 33 has been amended to delete the term "reagent-EphA2" and recite therefor antibody-EphA2, so as to correctly refer to the antecedent for this term in claim 1.

Claim 21 has been amended to recite detecting the presence of metastatic cells in a tissue sample; support for this amendment is found, for example, in the specification at page 4, lines 13-20. Claims 5 and 91 have been amended to correct a dependency.

Reconsideration and withdrawal of the rejections in view of the above amendments and the following comments is respectfully requested.

Information Disclosure Statements

Applicants have included copies of 1449 forms previously filed herein with information disclosure statements as Exhibit A (1 page, filed October 5, 2001 and considered December 10, 2001), Exhibit B (2 pages, filed and considered June 13, 2003), and Exhibit C (9 pages, filed and considered June 13, 2003). Applicants note that on the 1449 form entitled Exhibit A, one of the two citations was initialed by the Examiner and the other citation was not. The Office Action, dated January 2, 2002, with which this 1449 form was returned did not specify that the non-initialed citation was intentionally omitted from consideration.

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On the 1449 forms entitled Exhibits B and C, the first page of each set of 1449 forms was initialed at each citation, but none of the subsequent pages were initialed. These 1449 forms were returned with the current Office Action, dated June 19, 2003. This Office Action likewise did not specify that the non-initialed citations were intentionally omitted from consideration.

It is respectfully requested that the Examiner consider each of the documents cited on the 1449 forms of Exhibits A-C, and return copies of the 1449 forms with each citation initialed with the next official communication.

Rejoinder of Claims

The Examiner indicated that Group "V", "drawn to a method of detecting cancer cells" has been rejoined to elected Group I. Applicants thank the Examiner, and assume the Examiner meant Group IV (claims 72-81), which assumption is otherwise supported by the record (see, for example, Applicant's Amendment mailed October 5, 2001, requesting modification of the restriction requirement to combine Groups I and IV). The Examiner is requested to clarify the rejoinder if the Applicants' assumption is erroneous.

Allowed Claims

The Examiner indicated at line 5 of the Office Action Summary that claims 72, 73, 75-81, 90 and 91 are allowed.

However, at several places in the Office Action, some of these claims are also indicated as being rejected or objected to. For example, claim 91 is indicated as being objected to for informalities (paragraph 7 of the Office Action mailed June 19, 2003), and claims 90 and 91 are indicated as being rejected under 35 U.S.C. §112, second paragraph (at paragraph 8 of the Office Action mailed June 19, 2003). Claims 77 and 81 are indicated as being rejected under 35 U.S.C. §112, first paragraph.

Applicants have responded to the rejections and objections made in relation to the "allowed" claims in order to advance prosecution of the instant application. However, in view of the inconsistencies in the Office Action mailed June 19, 2003, Applicants request that if the pending claims are not found allowable, the next Office Action in this matter be made non-final to afford the Applicants a reasonable opportunity to address the remaining issues.

Rejection under 37 C.F.R. 1.75

Claims 30 and 31 are objected to under 37 C.F.R. 1.75 as being a substantial duplicate of claims 3 and 4, respectively. This rejection is traversed; however, claims 30 and 31 are canceled, rendering the rejection moot.

Claim 38 is objected to under 37 C.F.R. 1.75(c) as being of improper dependent form. This rejection is traversed; however, claim 38 is canceled, rendering the rejection moot.

Claims 3-7 are objected to because they are dependent upon canceled claim 2. This rejection is traversed; however, claims 3 and 5 are amended to correct the dependencies, thereby obviating the rejection with respect to these claims.

Claim 91 is objected to because it is dependent upon canceled claim 82. This rejection is traversed; however claim 91 has been amended to depend from claim 90, thereby obviating the rejection.

Reconsideration and withdrawal of the rejection under 37 C.F.R. 1.75 is respectfully requested.

Rejection under 35 U.S.C. §112, Second Paragraph

The Examiner rejected claims 1-13, 28, 30, 31, 33-46, 90 and 91 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the Examiner found claim 1 indefinite for failing to relate the step of detecting antibody-EphA2-binding to the

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claim objective, and found the phrase "reagent-EphA2-binding" in claim 33 as lacking antecedent basis. This rejection is respectfully traversed.

Claim 2 was previously canceled, and claims 28, 30, 31 and 38-40 are canceled herewith, rendering the rejection moot with respect to those claims.

Claim 1 has been amended to include the recitation of claim 28, "wherein antibody-EphA2 binding is indicative of the presence of metastatic cells in the cell population." It is respectfully submitted that this recitation relates detection of antibody –EphA2 binding to the objective of the claim, which as stated in the preamble is detecting the presence of metastatic cells in a cell population. Claim 28 has, accordingly, been canceled. It is submitted that the amendment to claim 1 obviates the rejection as it relates to claim 1 and the pending claims that depend, directly or indirectly, therefrom (claims 1, 3-13, 33-37 and 41-46). Applicants are unsure why this rejection was applied to claim 28 in the first place and respectfully request clarification if this was not an oversight on the Examiner's part and it is found that the amendment to incorporate the recitations of claims 28 to claim 1 does not obviate the rejection.

Claim 33 has been amended to delete recitation of "reagent-EphA2" binding and insert therefor "antibody-EphA2" binding, thereby obviating the rejection.

Reconsideration and withdrawal of the rejection of rejection of claims 1-13, 28, 30, 31, 33-46, 90 and 91 under 35 U.S.C. §112, second paragraph, is respectfully requested.

Rejection under 35 U.S.C. §112, First Paragraph

The Examiner rejected claim 51 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner did not find support in the specification for "extracellular" epitope.

Applicants traverse this rejection and respectfully direct the Examiner's attention to page 4, line 10, wherein it is disclosed that hybridoma B2D6 binds to an extracellular epitope.

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Reconsideration and withdrawal of the rejection of claim 51 under 35 U.S.C. §112, first paragraph, is respectfully requested.

The Examiner rejected claims 4, 31, 50, and 54, under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, it is asserted that all of the conditions of 37 C.F.R. §§ 1.801-1.809 were not met by the Declaration regarding the deposit of hybridoma cell line producing the antibody D7, filed in the instant application on March 24, 2003.

Initially, Applicants respectfully submit that claims 77 and 81 should also be considered with respect to the present rejection, and the following comments are applicable to these claims as well as claims 4, 31, 50 and 54. Also, please note that claim 31 has been canceled, rendering the rejection moot with respect to that claim.

Applicants submit that a Statement of Availability was filed with an Amendment and Response in the present application on May 30, 2002. A copy of the filed Statement of Availability is included herewith as Exhibit D. An amendment to the specification was also made in Amendment and Response filed May 30, 2002, to include information regarding the deposit of hybridoma D7 and hybridoma B2D6 with the American Type Culture Collection (ATCC). Additionally, a Declaration of Michael S. Kinch Under 37 C.F.R. §1.132, describing the circumstances of the deposit of hybridoma D7 was filed March 24, 2003. A copy of this submission is included herewith as Exhibit E.

Applicants further include herewith, labeled as Exhibit F, a copy of a Declaration of Michael S. Kinch Under 37 C.F.R. §1.132, filed in a related application, which describes the circumstances of the deposit of hybridoma B2D6 with the ATCC. Included with this Declaration is a copy of the Receipt from the ATCC regarding the deposit of hybridoma B2D6, indicated as ATCC No. PTA 2754. Applicants further include herewith, as Exhibit G, a copy of the Receipt from the ATCC regarding the deposit of hybridoma D7, indicated as ATCC No. PTA 2755.

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In view of the above comments and Exhibits D-G herein, Applicants respectfully submit that all required deposits have been made and that all conditions of 37 C.F.R. §§1.801-1.809 have been met. Reconsideration and withdrawal of the rejection of claims 4, 31, 50, and 54, under 35 U.S.C. §112, first paragraph, is, therefore, respectfully requested. In addition, if the Examiner finds that the provisions of the Budapest Treaty are still not fully satisfied, clarification regarding the remaining deficiencies is respectfully requested.

Rejection under 35 U.S.C. §102(b)

The Examiner rejected claims 47, 51, 52, 53, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, and 65 are rejected under 35 U.S.C. §102 (b) as being anticipated by Khan et al. *American Journal of Clinical Pathology* 1984;84:184-191, as evidenced by the abstract of Chen et al. (J. Biol. Chem. 1998, 273:24670-24675). Applicants respectfully traverse this rejection.

The claims recite "EphA2" which was, indeed, originally known as an epithelial cell kinase, i.e., "Eck." However, the "Eck" taught in Kahn et al. is an entirely different molecule, *towit*, an "epidermal cytokeratin." Khan et al. is there not relevant to the invention and should be removed as a reference.

Reconsideration and withdrawal of the rejection of claims 47, 51, 52, 53, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, and 65 under 35 U.S.C. §102 (b) as being anticipated by Khan et al. *American Journal of Clinical Pathology* 1984;84:184-191 is therefore respectfully requested.

The Examiner rejected claims 1, 3, 5, 11, 21, 23, 28, 30, 33, 35, 37, 38, 40, 41, 45, 47, 49, 52, 55, 56, 58, 60, 61, 63, 64, and 68 under 35 U.S.C. §102(b) as being anticipated by Easty et al. (International Journal of Cancer, 1995;60:129-136) as evidenced by the abstract of Chen et al. *Journal of Biological Chemistry* 1998, 273 24670-24675 and Lindberg et al. *Molecular and Cellular Biology*, 1990;10:6316-6324. It is respectfully submitted that the cancellation of claim 3 renders the rejection of this claim moot. As to claims 1, 5, 11, 21, 23, 28,

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30, 33, 35, 37, 38, 40, 41, 45, 47, 49, 52, 55, 56, 58, 60, 61, 63, 64, and 68, Applicants respectfully traverse this rejection.

For a claim to be anticipated under 35 U.S.C. §102(b), each and every element of the claim must be found in a single prior art document (M.P.E.P. §2131). Applicants assert that Easty et al. fail to teach each and every element of independent claims 1, 21, and 47.

Claims 1 and 47 are directed to methods for detecting the presence of metastatic cells in a cell population that include, *inter alia*, incubating cells with a monoclonal antibody that specifically binds EphA2 (emphasis added). Easty et al. teach a polyclonal anti-EphA2 antibody, but, contrary to the assertion of the Examiner, fail to teach an anti-EphA2 monoclonal antibody. Easty et al. therefore, fail to teach each and every element of claims 1 and 47, and claims 3, 5, 11, 28, 30, 33, 35, 37, 38, 40, 41, 45, 49, 52, 55, 56, 58, 60, 61, 63, 64, and 68, dependent directly or ultimately thereto.

Claim 21, as amended, is directed to a method for detecting the presence of metastatic cells in a tissue sample which includes incubating the tissue sample with a reagent capable of specific binding to a nucleic acid coding for the EphA2 protein to allow reagent binding to the nucleic acid, and detecting reagent-nucleic acid binding. Reagent-nucleic acid binding is indicative of the presence of metastatic cells in the tissue sample.

Easty et al. do not teach the detection of a nucleic acid coding for the EphA2 protein in a tissue sample. Therefore Easty et al. do not anticipate the invention of claim 21 or any claim dependent therefrom.

Reconsideration and withdrawal of the rejection of claims 1, 3, 5, 11, 21, 23, 28, 30, 33, 35, 37, 38, 40, 41, 45, 47, 49, 52, 55, 56, 58, 60, 61, 63, 64, and 68 under 35 U.S.C. §102(b) as being anticipated by Easty et al. as evidenced by the abstract of Chen et al. and Lindberg et al. is respectfully requested.

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Summary

It is respectfully submitted that the pending claims 1, 3-13, 21, 23, 24, 28, 30, 31, 33-47, 49-69, 72, 73, 75-81, and 90-93 are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted for
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CERTIFICATE UNDER 37 CFR §1.10:

"Express Mail" mailing label number: EV073736811US

Date of Deposit: 19 December 2003

The undersigned hereby certifies that this paper is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR §1.10 on the date indicated above and is addressed to the Assistant Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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